



SEQUENCE LISTING

<110> Genzyme Corporation
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<120> Methods of Treating Diabetes and Other Blood Sugar Disorders

<130> 5121

<140> US 10/715,976

<141> 2003-11-17

<160> 54

<170> PatentIn version 3.2

<210> 1

<211> 158

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of SEAP.GLP-1Gly8

<400> 1

gaattccgcc caccatgctg ctgctgctgc tgctgctggg cctgcgcctg cagctgagcc 60

tgggccacgg cgagggcacc ttcaccagcg acgtgagcag ctacctggag ggccaggccg 120

ccaaggagtt catgcctgg ctggtgaagg gccgcggc 158

<210> 2

<211> 48

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of SEAP.GLP-1Gly8

<400> 2

Met Leu Leu Leu Leu Leu Leu Gly Leu Arg Leu Gln Leu Ser Leu
1 5 10 15

Gly His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
20 25 30

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
35 40 45

<210> 3

<211> 250

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of Exendin-4.GLP-1Gly8

<400> 3

gaattccgcc caccatgaag atcatcctgt ggctgtgtgt gttcggcctg ttcctggcca 60

ccctgttccc catcagctgg cagatgcccg tggagtccgg cctgtcctcc gaggactccg 120

ccagctccga gagcttcgcc aagcgcatca agcgccacgg cgagggcacc ttcaccagcg 180
acgtgagcag ctacctggag ggccaggccg ccaaggagtt catcgcttgg ctggtgaagg 240
gccgcggctg 250

<210> 4
<211> 78
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of Exendin-4.GLP-1Gly8

<400> 4

Met Lys Ile Ile Leu Trp Leu Cys Val Phe Gly Leu Phe Leu Ala Thr
1 5 10 15

Leu Phe Pro Ile Ser Trp Gln Met Pro Val Glu Ser Gly Leu Ser Ser
20 25 30

Glu Asp Ser Ala Ser Ser Glu Ser Phe Ala Lys Arg Ile Lys Arg His
35 40 45

Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln
50 55 60

Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
65 70 75

<210> 5
<211> 245
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence of Helodermin.GLP-1Gly8

<400> 5

gaattccgcc caccatgaag agcatcctgt ggctgtgtgt gtttggcctg ctgattgcca 60
ccctgttccc tgtgagctgg cagatggcca tcaagagcag actgtcctct gaggactctg 120
agacagacca gagactgaag cgcacaaagc gccacggcga gggcaccttc accagcgacg 180
tgagcagcta cctggagggc caggccgcca aggagttcat cgcctggctg gtgaagggcc 240
gcggc 245

<210> 6
<211> 77
<212> PRT
<213> Amino acid sequence of Helodermin.GLP-1Gly8

<400> 6

Met Lys Ser Ile Leu Trp Leu Cys Val Phe Gly Leu Leu Ile Ala Thr
1 5 10 15

Leu Phe Pro Val Ser Trp Gln Met Ala Ile Lys Ser Arg Leu Ser Ser
 20 25 30

Glu Asp Ser Glu Thr Asp Gln Arg Leu Lys Arg Ile Lys Arg His Gly
 35 40 45

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
 50 55 60

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
 65 70 75

<210> 7
 <211> 260
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide sequence of GIP.GLP-1Gly8

<400> 7
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 tggctgtggg actgggcgag aagaaggaag gccacttcag cgccctgccc agcctgccag 120
 tgggcagcca tgccaaggtg agctccccac agaagcgcac caagcgccac ggcgagggca 180
 ccttcaccag cgacgtgagc agctacctgg agggccaggc cgccaaggag ttcacgcct 240
 ggctggtgaa gggccgcggc 260

<210> 8
 <211> 82
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence of GIP.GLP-1Gly8

<400> 8

Met Val Ala Thr Lys Thr Phe Ala Leu Leu Leu Ser Leu Phe Leu
 1 5 10 15

Ala Val Gly Leu Gly Glu Lys Lys Glu Gly His Phe Ser Ala Leu Pro
 20 25 30

Ser Leu Pro Val Gly Ser His Ala Lys Val Ser Ser Pro Gln Lys Arg
 35 40 45

Ile Lys Arg His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
 50 55 60

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
 65 70 75 80

Arg Gly

<210> 9
 <211> 266
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide sequence of IGF-1 (furin).GLP-1Gly8

<400> 9
 gaattccgcc caccatgggc aagatcagca gcctgccac ccagctgttc aagtgtgct 60
 tttgtgactt cctgaagggtg aagatgcaca ccatgagctc cagccacctg ttctacctgg 120
 ccctgtgcct gctgaccttc accagctccg ccacagccaa gcgcatcaag cgccacggcg 180
 agggcacctt caccagcgac gtgagcagct acctggaggg ccaggccgcc aaggagttca 240
 tcgcctggct ggtgaagggc cgcggc 266

<210> 10
 <211> 84
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino sequence of IGF-1 (furin).GLP-1Gly8

<400> 10
 Met Gly Lys Ile Ser Ser Leu Pro Thr Gln Leu Phe Lys Cys Cys Phe
 1 5 10 15
 Cys Asp Phe Leu Lys Val Lys Met His Thr Met Ser Ser Ser His Leu
 20 25 30
 Phe Tyr Leu Ala Leu Cys Leu Leu Thr Phe Thr Ser Ser Ala Thr Ala
 35 40 45
 Lys Arg Ile Lys Arg His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser
 50 55 60
 Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
 65 70 75 80
 Lys Gly Arg Gly

<210> 11
 <211> 251
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide sequence of IGF-1.GLP-1Gly8

<400> 11
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 tttgtgactt cctgaagggtg aagatgcaca ccatgagctc cagccacctg ttctacctgg 120
 ccctgtgcct gctgaccttc accagctccg ccacagccca cggcgagggc accttcacca 180

gcgacgtgag cagctacctg gagggccagg ccgccaagga gttcatcgcc tggctggtga 240
 agggccgcgg c 251

<210> 12
 <211> 79
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence of IGF-1.GLP-1Gly8

<400> 12

Met Gly Lys Ile Ser Ser Leu Pro Thr Gln Leu Phe Lys Cys Cys Phe
 1 5 10 15

Cys Asp Phe Leu Lys Val Lys Met His Thr Met Ser Ser Ser His Leu
 20 25 30

Phe Tyr Leu Ala Leu Cys Leu Leu Thr Phe Thr Ser Ser Ala Thr Ala
 35 40 45

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 50 55 60

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
 65 70 75

<210> 13
 <211> 167
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide sequence of Preproglucagon.GLP-1Gly8

<400> 13

gaattccgcc caccatgaaa agcatttact ttgtggctgg gctgtttgtg atgctggtgc 60

aaggcagctg gcaacacggc gagggcacct tcaccagcga cgtgagcagc tacctggagg 120

gccaggccgc caaggagttc atgcctggc tggatgaagg ccgcggc 167

<210> 14
 <211> 51
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence of Preproglucagon.GLP-1Gly8

<400> 14

Met Lys Ser Ile Tyr Phe Val Ala Gly Leu Phe Val Met Leu Val Gln
 1 5 10 15

Gly Ser Trp Gln His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser
 20 25 30

Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys
 35 40 45

Gly Arg Gly
 50

<210> 15
 <211> 179
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide sequence of Alpha-1 antitrypsin.GLP-1Gly8

<400> 15
 gaattccgcc caccatgccc tcttctgtct cctggggcat cctcctgctg gcaggcctgt 60
 gctgcctggt cctgtctcc ctggctcacg gcgagggcac cttcaccagc gacgtgagca 120
 gctacctgga gggccaggcc gccaaaggagt tcatcgcttg gctggtgaag ggccgcggc 179

<210> 16
 <211> 55
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence of Alpha-1 antitrypsin.GLP-1Gly8

<400> 16

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys
 1 5 10 15

Cys Leu Val Pro Val Ser Leu Ala His Gly Glu Gly Thr Phe Thr Ser
 20 25 30

Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala
 35 40 45

Trp Leu Val Lys Gly Arg Gly
 50 55

<210> 17
 <211> 245
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide sequence of Factor IX.GLP-1Gly8

<400> 17
 gaattccgcc caccatgcag agagtgaaca tgatcatggc agaatcccca ggcctgatca 60
 ccatctgcct cctgggatac ctctgtctg ctgagtgcac agtggtcctg gaccatgaga 120
 atgccaacaa gattctgaac agaccaaga ggcattggga gggcaccttc accagcgacg 180
 tgagcagcta cctggagggc caggccgcca aggagttcat cgcctggctg gtgaagggcc 240
 gcggc 245

<210> 18
 <211> 77
 <212> PRT
 <213> Artificial

<220>
 <223> Amino acid sequence of Factor IX.GLP-1Gly8

<400> 18

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
 1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
 20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg His Gly
 35 40 45

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
 50 55 60

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
 65 70 75

<210> 19
 <211> 254
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide sequence of Exendin-4 (IGF-1).GLP-1Gly8

<400> 19
 gaattccgcc caccatgaag atcatcctgt ggctgtgtgt gttcggcctg ttcctggcca 60
 ccctgttccc catcagctgg cagatgcccg tggagtccgg cctgtcctcc gaggactccg 120
 ccagctccga gagccctctg aagcctgcca agtctgccag acatggagag ggcaccttca 180
 catctgacgt gaggagctac ctggagggcc aggccgccaa ggagttcatc gcctggctgg 240
 tgaagggccg cggc 254

<210> 20
 <211> 80
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence of Exendin-4 (IGF-1).GLP-1Gly8

<400> 20

Met Lys Ile Ile Leu Trp Leu Cys Val Phe Gly Leu Phe Leu Ala Thr
 1 5 10 15

Leu Phe Pro Ile Ser Trp Gln Met Pro Val Glu Ser Gly Leu Ser Ser
 20 25 30

Glu Asp Ser Ala Ser Ser Glu Ser Pro Leu Lys Pro Ala Lys Ser Ala
35 40 45

Arg His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
50 55 60

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
65 70 75 80

<210> 21
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> GLP-1(7-37)

<400> 21

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 22
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; Gly8-GLP-1 (7-37)

<400> 22

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 23
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (7-34)

<400> 23

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys
20 25

<210> 24
<211> 29

<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (7-35)

<400> 24

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
20 25

<210> 25
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (7-36)

<400> 25

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 26
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; Val8-GLP-1 (7-37)

<400> 26

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 27
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; Gln9-GLP-1 (7-37)

<400> 27

His Ala Gln Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 28
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; Thr16-Lys18-GLP-1 (7-37)

<400> 28

His Ala Glu Gly Thr Phe Thr Ser Asp Thr Ser Lys Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 29
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; Lys18-GLP-1 (7-37)

<400> 29

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Lys Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 30
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; D-Gln9-GLP-1 (7-37)

<400> 30

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Gln Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 31
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (2-37)

<400> 31

Asp Glu Phe Glu Arg His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser
1 5 10 15

Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
20 25 30

Lys Gly Arg Gly
35

<210> 32
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (3-37)

<400> 32

Glu Phe Glu Arg His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser
1 5 10 15

Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys
20 25 30

Gly Arg Gly
35

<210> 33
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (6-37)

<400> 33

Arg His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
1 5 10 15

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 34
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Recognition site for furin cleavage

<220>
<221> misc_feature
<222> (2)..(2)
<223> Xaa can be any naturally occurring amino acid

<400> 34

Arg Xaa Lys Arg
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<210> 35

<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Recognition site for furin cleavage

<220>
<221> misc_feature
<222> (2)..(2)
<223> Xaa can be any naturally occurring amino acid
<400> 35

Arg Xaa Arg Arg
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<210> 36
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Recognition site for furin cleavage

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa can be either Lys or Arg

<220>
<221> misc_feature
<222> (3)..(3)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa can be either Lys or Arg

<400> 36

Xaa Arg Xaa Xaa Arg
1 5

<210> 37
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Recognition site for furin cleavage

<220>
<221> misc_feature
<222> (2)..(3)
<223> Xaa can be any naturally occurring amino acid

<400> 37

Arg Xaa Xaa Arg
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<210> 38
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Recognition site for furin cleavage

<400> 38

Arg Gln Lys Arg
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<210> 39
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> IGF-1 signal sequence

<400> 39

Pro Leu Lys Pro Ala Lys Ser Ala Arg
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<210> 40
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 40

Pro Leu Lys Pro Ala Lys Ser Lys Arg
1 5

<210> 41
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 41

Pro Leu Lys Pro Ala Arg Ser Ala Arg
1 5

<210> 42
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 42

Pro Leu Arg Pro Ala Lys Ser Ala Arg
1 5

<210> 43
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 43

Pro Leu Ala Pro Ala Lys Ser Ala Arg
1 5

<210> 44
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-signal 1 sequence

<400> 44

Pro Leu Lys Pro Ala Arg Ser Lys Arg
1 5

<210> 45
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 45

Pro Leu Arg Pro Ala Lys Ser Lys Arg
1 5

<210> 46
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 46

Pro Leu Arg Pro Ala Arg Ser Lys Arg
1 5

<210> 47
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 47

Pro Leu Ala Pro Ala Lys Ser Lys Arg
1 5

<210> 48
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 48

Pro Leu Ala Pro Ala Arg Ser Lys Arg
1 5

<210> 49
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 49

Pro Leu Ala Pro Ala Arg Ser Ala Arg
1 5

<210> 50
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 50

Pro Leu Arg Pro Ala Arg Ser Ala Arg
1 5

<210> 51
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> 5705DA

<400> 51
ttctacacac cccgctccaa gcgtgaagtg gag

33

<210> 52
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> 5706DA

<400> 52
gtcctccact tcacgcttgg agcggggtgt

30

<210> 53

<211> 51
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Annealed oligonucleotides containing a polylinker for cloning

 <400> 53
 gatctcctag gggtttcgaa accactagta agcttaccgc atgccttaag g 51

 <210> 54
 <211> 51
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Annealed oligonucleotides containing a polylinker for cloning

 <400> 54
 ctagccttaa ggcattgcggt aagcttacta gtggtttcga aacccttagg a 51